REMARKS

The Examiner objected to claims 1, 12-13, 15, and 27 because of the presence of a period after the word "identifiers". Claim 1 has been amended, curing the defect.

The Examiner rejected claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 under 35 U.S.C. 102(b) as being anticipated by Cuticchia et al. [CABIOS, 1992, volume 8, pages 467-474]. Applicant submits that as currently amended, claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 are not anticipated by Cuticchia

Claim 1 is drawn to a computer-implemented method for overlaying gene- or protein-related data on chromosome maps to provide at least one data-enhanced chromosome map as output. As currently amended, the claimed method comprises six major steps involving automated data input, manipulation and display.

First, claim 1 requires that chromosome maps be **received as a first input**. The Examiner points to the first two paragraphs of the subsection "System and methods" beginning on Page 467 as providing this teaching. The cited paragraphs discuss two standard database systems, and some hardware and software details on the Rdb product used by Cuticchia, but does not teach the input of any chromosome maps. Cuticchia teaches (Abstract) that "information about DNA fragments" may be organized to ***create*** a physical map which can subsequently be updated as more data is gathered. Cuticchia achieves this using a "software package supporting a data base for both the ***production*** and storage of a physical map" which may be of the contig or chromosome-walk types. Hence, at most, Cuticchia provides a chromosome map as an output, rather than receiving a chromosome map as an input.

Second, the sixth step of claim 1 requires that the data items received in the second claimed step be displayed on one of the chromosome maps to provide a data-enhanced chromosome map as an output. The Examiner points to Figure 1, apparently identifying the 2D matrix of circles that may be filled as the recited chromosome map which is "enhanced" by the

black, grey or white fills. However, Figure 1 does not show any chromosome map. Indeed, Cuticchia teaches (page 460, left column) that the displayed 2D matrix of circles is simply a "representation of the microtitre plate" in which experiments have been performed, so that the user may fill in the experimental hybridization result from a given well in the array by pointing and clicking a cursor at the position corresponding to that well. Applicant finds no teaching anywhere in Cuticchia of the display of a data-enhanced chromosome map, as required by the claim.

Hence, Cuticchia does not teach the claim limitations either with regard to the recited inputs or with regard to the desired output.

Third, claim 1 requires that an identifier specifying a genetic location on said chromosome maps for each of a list of data items comprising data other than data specifying a genetic location on said chromosome maps be provided. Applicant finds no teaching in Cuticchia of the provision of such identifiers.

Fourth, claim 1 requires that the computer match the identifiers to predetermined identifiers on at least one of said chromosome maps. Cuticchia does not teach such matching. At most, Figure 1 of Cuticchia teaches the matching of hybridization data to row-column positions of the wells in a microtitre plate at which those hybridization data were obtained. As noted above, the representation of a microtitre plate is not a chromosome map.

Fifth, claim 1 requires that the computer reorder the data items to an order matching the order of said predetermined identifiers. Cuticchia does not teach such reordering.

Accordingly, Applicant submits that claim 1 and the claims dependent therefrom are not anticipated by Cuticchia.

Claim 3 depends from claim 1 and additionally requires that said gene- or protein-related data be spatially grouped to correspond to spatial groupings of said associated genes on said at

least one chromosome map. The Examiner points to Figure 1 on page 468 of Cuticchia as teaching this grouping, identifying the black/grey/white fills of the circles shown as the data. As noted above with respect to claim 1, Figure 1 is a representation of a microtitre plate, not a chromosome. The spots on the plate represent the hybridization of genetic material in a sample with known genes. However, the genes are not necessarily even from the same chromosome. Moreover, the filling in of circles corresponding to particular wells in the plate is not equivalent to any spatial *grouping*. Hence, there are additional grounds for allowing claim 3.

Claim 12 depends from claim 1 and additionally requires in part that the identifiers **specifying a genetic location for each of said data items** be **matched** with specific information in an accessed **external source** of information relative to the data displayed, wherein said specific information comprises data other than markers, identifiers, or a chromosome map. Cuticchia does not provide this teaching. Hence, there are additional grounds for allowing claim 12.

Claim 13 depends from claim 1 and additionally requires that the identifiers **specifying a genetic location for each of said data items** be selected from published gene identifiers and symbols. Cuticchia does not provide this teaching. Hence, there are additional grounds for allowing claim 13 and the claims dependent therefrom.

Claim 15 depends from claim 1 and additionally requires that said matching comprise providing a relational database which stores a set of cross-referenced **tables for matching said identifiers with said predefined identifiers,** and as the identifiers are read, they are matched with said predefined identifiers in the cross-referenced tables through standard database queries. Cuticchia does not provide this teaching. Hence, there are additional grounds for allowing claim 15.

Claim 20 depends from claim 1 and additionally requires that co-location values be statistically assessed and that assessed co-location statistical significance be displayed along side said gene- or protein-related data. The Examiner looks to Figure 1 of Cuticchia and the

discussion in the second column of page 468 as providing the teaching in question. Applicant must disagree with the Examiner's reading of the passage in question. The value of d(a,b) measures the difference in hybridization values between two different clones. It does not measure any measure of co-location of genes on a chromosome. Again, the data being analyzed in Cuticchia does not even need to come from the same chromosome. Accordingly, there are additional grounds for allowing Claim 20.

Claim 21 depends from claim 1 and additionally requires that additional information characterizing the gene- or protein-related data be displayed along side of said display of that data and positioned relative to the respective locations on the chromosome map of the respective genes characterized by that data. Cuticchia teaches (full paragraph in column 2 on page 468) the calculation of degrees of similarity of hybridization profiles, but Applicant finds no teaching that the calculated values are displayed on any chromosome map, let alone in the manner recited in the claim. Hence, there are additional grounds for allowing claim 21 and the claims dependent therefrom.

Claim 24 depends from claim 21 and additionally requires that the additional information be selected from the group consisting of CGH data, protein levels, relevance scores and relevance densities. The Examiner interprets the hybridization data of Figure 1 of Cuticchia as relevance scores. At best, the hybridization data can be used to compute relative protein levels for specific proteins. However, there is no teaching of displaying the hybridization data on a chromosome map. Hence, there are additional grounds for allowing claim 24.

Claim 26 requires that the gene or protein related data is displayed in a scatter plot format. The Examiner looks to Figures 1 and 5 of Cuticchia as teaching such scatter plots. First, Figure 1 is not a scatter plot, it is a display of the hybridization data on a number of hybridization plates. Second, the issue is not whether a scatter plot is known, but rather, whether Cuticchia teaches displaying gene or protein related data received in the list of Claim 1 on a chromosome map as a scatter plot. The scatter plot in Figure 5 displays data calculated by the program for different clones, but this display is hardly on a chromosome map. Hence, there are additional

grounds for allowing Claim 26.

Claim 27 requires that the gene or protein related data be imported form a plurality of experiments. The Examiner points to Figure 1 of Cuticchia as providing the teaching in question. Applicant must respectfully disagree with the Examiner's reading of the reference. Figure 1 is data from a heat map showing hybridization results from a plurality of experiments. Again, the issue is not whether the reference teaches inputting data from a plurality of experiments, but rather whether that data is displayed in the claimed manner. The Examiner has not pointed to any teaching of displaying data in the claimed manner. Hence, there are additional grounds for allowing Claim 27, and the claims dependent therefrom.

Claim 29 requires that additional information including at least one of annotations, cellular localization of the genetic material, cluster data, and statistical data be displayed on the chromosome map. The Examiner again looks to Figure 1 has providing that data. The data in Figure 1 is heat map. While this data does include annotations, this data the degree to which the sample nucleic acid binds to each of a number of probes. This data is not displayed on a chromosome map.

Claim 55 depends from claim 1 and has additional limitations similar to those of claim 21 except that the additional information displayed is related to one or more genes characterized by said gene- or protein-related data. Applicant submits that the same additional grounds exist for allowing claim 55 and the claims dependent therefrom as in the case of claim 21, discussed above.

The Examiner rejected claims 4-11 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Koleszar et al. [US Patent 6,519,583; issued 11 February 2003; filed 27 July 1999]. Applicant submits that as currently amended, claims 4-11 are not obvious in view of the cited prior art.

The Examiner states that Cuticchia teaches the limitations of claims 4-11, except for the limitations requiring particular display features. The Examiner looks to Koleszar, whose teachings are directed towards the graphical display of computer-based biomolecular sequence information for the missing teachings. The Examiner maintains that it would have been obvious to apply the display features taught by Koleszar to the method of Cuticchia to display "the genomic data in a more convenient and user-friendly format [see, for example, column 2, lines 5-9 of Koleszar et al.]".

As noted above with respect to claim 1, from which claims 4-11 depend, Cuticchia does not teach the base claim limitations regarding the recited inputs, the desired output, identifiers, identifier matching, and data reordering. Koleszar does not provide the missing teachings. Accordingly, Applicant submits that claims 4-11 are not obvious in view of the cited prior art.

Furthermore, Koleszar teaches zooming in and out on sequence data. The Examiner points to Figure 1 of Cuticchia as the chromosome map on which the other data is displayed. Hence, the combination of the references would lead to a zoom feature on Figure 1. However, there is no detail in Figure 1 that is not visible from the current Figure 1. Hence, nothing is gained by providing the zoom feature of Koleszar to the display of Cuticchia. Accordingly, there are additional grounds for allowing Claims 4 and 5.

With respect to claim 6, consider the additional requirement that information on the display that a user is not interested in viewing be queried and cut. In the current office action, the Examiner points to the Abstract and Figure 4B of Koleszar as providing this teaching. Applicant finds no teaching in the cited passage or figure regarding querying and cutting as specified. The issue is not whether interlinked views may be shown on one display, but whether querying and cutting are intrinsically or inherently involved. Applicant respectfully submits that they are not. Hence, there are additional grounds for allowing claim 6.

Claim 7 requires a plurality of chromosome maps and limitations with respect to the maintaining focus and context within that display. The Examiner has not pointed to any teaching

of a display with multiple chromosome maps in either reference, no less that the require display techniques are performed in either reference. Hence, there are additional grounds for allowing Claim 7.

Claim 8 depends from claim 1 and additionally requires that a high level view of all of said chromosome maps and gene- or protein-related data, a mid-level view displaying a magnified view of a selected portion of said high level view, and a detailed view displaying expanded, detailed information characterizing a selected portion of said mid-level view be simultaneously displayed. In the current office action, the Examiner points to Figure 4B of Koleszar as providing this teaching. At most, the cited figure shows two views of a gene map in the top and middle panels of the display, not three. Koleszar teaches (column 12, line 63-column 13, line 19) that the third panel 450 of the graphical viewer 402 is the sequence depth viewer 452, which shows a graph of "*depth of coverage information*", not a chromosome map. Hence, there are additional grounds for allowing claim 8 and the claims dependent therefrom.

Claim 9 depends from claim 8 and additionally requires that said high-level view, mid-level view and detailed view all be interlinked so that changing one view automatically changes the other two views in the same way, substantially simultaneously. The Examiner has not pointed to any teaching that discloses these details. Furthermore, Applicant finds no teaching in Figure 4B or elsewhere in Koleszar that even two views are interlinked so that changing one view automatically changes the other two views in the same way, substantially simultaneously. Hence, there are additional grounds for allowing claim 9.

Claim 11 depends from claim 1 and additionally requires that popup dialogs be displayed to display additional details relative to a selected portion of the display. The Examiner points to "pop-up buttons" in Figure 4A of Koleszar stating that these buttons are "interpreted to be pop-up menus". Applicant maintains that there is no teaching in Koleszar that activation of any of the cited buttons results in the **display of additional details relative to a selected portion of the display**. Hence, there are additional grounds for allowing claim 11.

The Examiner rejected claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. as applied to claims 1-3, 12-13, 15, 20-22, 24, 26-29, and 55-56 above in further view of Schena et al. [PNAS, 1996, volume 93, pages 10614-10619]. Applicant submits that as currently amended, claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 are not obvious in view of the cited prior art.

The Examiner states that Cuticchia teaches all the limitations of base claim 1, from which claims 14, 16-19, 23, 25, 30-37, 40-43 depend, and most of the limitations of base claim 80, looking to Schena for the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of Schena to those of Cuticchia "because both studies analogously pertain to viewing data regarding chromosomal properties in the form of matrices".

First, as noted above with respect to claim 1, Cuticchia does not teach the limitations common to claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 regarding the recited inputs, the desired output, identifiers, identifier matching, and data reordering. Schena does not provide the missing teachings.

Second, Applicant disagrees with the Examiner's reading of Cuticchia as pertaining to "to viewing data regarding chromosomal properties in the form of matrices". As noted above with regard to claim 1, the data viewed in Cuticchia in the cited figures does not include chromosomal properties in the form of matrices, but pictorial representations of microtitre plate wells which pertain to the expression of specific genes.

Accordingly, Applicant submits that claims 14, 16-19, 23, 25, 30-37, 40-43, 80-83, and 86-89 are not obvious in view of the cited prior art.

As noted above with respect to claim 21, from which claim 23 depends, Cuticchia does not teach the additional requirement that **additional information** characterizing the gene- or protein-related data be displayed along side of said display of that data and positioned relative to the respective locations on the chromosome map of the respective genes characterized by that

data. Schena does not provide the missing teachings. Hence, there are additional grounds for allowing claim 23 and the claims dependent therefrom.

Claim 30 depends from claim 18 and additionally requires that **row vectors of the values in the rows of the matrix be calculated;** using an auxiliary process to obtain cluster data for said row vectors; and displaying said cluster data along side said display of said arbitrary gene- or protein-related data. The Examiner points to Figures 1 and 2 of Schena, interpreting the left panel Figure 2 as showing cluster data obtained from the values in Figure 1. First, the Examiner has not pointed to any teaching that the data in Figure 2 represents any row vectors. Second, the display alongside the left panel of Figure 2 is another display of "cluster data" from a second experiment, not the data from which the left panel data was calculated. Hence, there are additional grounds for allowing claim 30 and the claims dependent therefrom.

Claims 32 and 33 depend from claim 30 and additionally require that cluster data be displayed in a single column or a multi-column matrix respectively, adjacent each matrix of gene- or protein-related data. Applicant finds no teaching of a data display in either a single column or a multi-column matrix adjacent a matrix of gene- or protein-related data in Schena. Hence, there are additional grounds for allowing claims 32 and 33.

Claim 34 depends from claim 1 and additionally requires that the gene- or protein-related data comprises a matrix of at least one microarray of gene expression data, wherein **each row of the matrix is associated with a particular gene, and wherein each column of the matrix is associated with a microarray experiment**, wherein a portion of the total number of columns are associated with experiments taken **from normal, healthy tissue**, and another portion of the total number of columns are associated with experiments taken **from tissue exhibiting an abnormality**, said method further comprising dividing the matrix into two smaller matrices with **a first matrix containing the columns associated with normal experiments and a second matrix containing the columns associated with abnormal experiments,** and wherein said matching and displaying are performed with regard to both first and second matrices.

The Examiner points to Figure 1 of Schena, identifying the left and right arrays as the first and second matrices. First, Schena does not teach that these arrays were initially combined as a single array. Indeed, as the experiment involved "heat shock" treatment, with the two arrays subjected to very different environmental conditions, they could not have been part of a single microarray experiment. Second, Schena does not teach that the "- Heat Shock" samples were taken from normal healthy tissue while the "+ Heat Shock" samples were taken from tissues exhibiting an abnormality. The only "abnormality" involved is the heat treatment applied as an experimental variable. Hence, there are additional grounds for allowing claim 34 and the claims dependent therefrom.

Claim 36 depends from claim 34 and additionally requires that a relevance score be calculated for at least one row of the matrices by comparing expression values in the first matrix with expression values in the second matrix, and displaying at least one calculated relevance score along side the row to which each pertains. The Examiner identifies the differential expression profiles in Figure 2A of Schena as relevance scores. First, as noted above with respect to claim 24, the current invention teaches that the term "relevance score", equivalent to the term "- log p value" is a measure of *the separation value of the particular gene being analyzed.* The profiles in Figure 2A of Schena are not quantitative measures that could be interpreted to be the recited scores. Hence, there are additional grounds for allowing claim 36 and the claims dependent therefrom.

Claim 41 depends from claim 36 and additionally requires that relevance scores be calculated and displayed in a binary code. The Examiner points to the binary codes in Table II in column 1 on page 472 of Cuticchia as providing this teaching. These codes are simply representations of the results of hybridization experiments. They are not the results of any calculation, let alone the calculation of relevance scores. Hence, there are additional grounds for allowing claim 41.

Claim 42 depends from claim 36 and additionally requires that a plurality of relevance scores be calculated, said method further comprising **defining a relevance density score** based

upon **distances between genetic locations and relevance scores**, and identifying **chromosomal locations** containing relevance density scores greater than or equal to the defined relevance density score. The Examiner points to Figure 1 of Cuticchia as providing these teachings, identifying the shadings of the circles as intervals of density scores. First, the shadings represent the presence of hybridization, the absence of hybridization, and the absence of a clone. No densities are involved. Second, the "hybridization distances d(a,b)" represent differences between profiles, not distances between genetic locations and relevance scores. Third, the locations indicated in the figure are not chromosomal locations. Hence, there are additional grounds for allowing claim 42

Claim 43 depends from claim 36 and additionally requires that the relevance scores be filtered by setting at least one relevance score limit value and displaying only those relevance scores which are greater than or equal to at least one relevance score limit value. The Examiner points to Figure 2 of Schena as providing this teaching. The legend teaches that some data values were not shown, based on the relative spread of results between two experiments. This is not equivalent to teaching exclusion based on a simple threshold value, let alone on a relevance score limit value. Hence, there are additional grounds for allowing claim 43.

As the Examiner notes, claim 80 is drawn to similar subject matter as dependent claim 34, including requirements discussed above with respect to claim 34, specifying details regarding the row and column data, normal and abnormal tissue, and the matching and displaying being performed with regard to two matrices that are divided out from a single original matrix. As noted above with respect to claim 80, Schena does not provide these teachings. Hence, there are additional grounds for allowing claim 80 and the claims dependent therefrom.

Claim 82 depends from claim 80 and additionally includes the same requirements as those of claim 36, regarding relevance scores. Applicant submits that the same additional grounds exist for allowing claim 82 and the claims dependent therefrom as those discussed above with respect to claim 36.

Claim 87 depends from claim 82 and additionally includes the same requirements as those of claim 41 regarding the calculation and display of relevance scores in a binary code. Applicant submits that the same additional grounds exist for allowing claim 82 as those discussed above with respect to claim 41.

Claims 88 and 89 depend from claim 82 and additionally include the same requirements as claims 42 and 43 respectively regarding relevance density scores and filtering and display of relevance scores. Applicant submits that the same additional grounds exist for allowing claims 88 and 89 as those discussed above with respect to claims 42 and 43 respectively.

The Examiner rejected claims 38 and 84 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982]. Applicant submits that as currently amended, claims 38 and 84 are not obvious in view of the cited prior art.

The Examiner states that the combination of Cuticchia and Schena teaches all the limitations of claims 38 and 84 except for requiring that the relevance score comprise a "p value" and the relevance score be displayed as a valued calculated by (-log p value). The Examiner looks to McCully for the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of McCully to those of Cuticchia/Schena to provide “improved and more advanced statistical analysis”.

First, as noted above with respect to claims 1 and 80, from which claims 38 and 84 respectively depend, the combination of Cuticchia and Schena fails to teach the limitations regarding the recited inputs, the desired output, identifiers, identifier matching, and data reordering. McCully does not provide the missing teachings.

Second, as noted above with respect to claims 36 and 82, from which claims 38 and 84 respectively also depend, the combination of Cuticchia and Schena fails to teach the requirement

that a relevance score be calculated for at least one row of the matrices by comparing expression values in the first matrix with expression values in the second matrix, and displaying at least one calculated relevance score along side the row to which each pertains. McCully does not provide the missing teachings.

Accordingly, Applicant submits that claims 38 and 84 are not obvious in view of the cited prior art.

The Examiner rejected claims 39 and 85 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378]. Applicant submits that as currently amended, claims 39 and 85 are not obvious in view of the cited prior art.

The Examiner states that the combination of Cuticchia and Schena teaches all the limitations of claims 39 and 85 except for the calculation of a plurality of relevance scores and their display as a line map. The Examiner looks to Ben-Dor for the missing teachings. The Examiner maintains that it would have been obvious to apply the teachings of Ben-Dor to the method of Cuticchia/Schena as "*an alternate means of analyzing the mappings of chromosomes*".

First, as noted above with respect to claims 36 and 82, from which claims 39 and 85 respectively depend, the combination of Cuticchia and Schena fails to teach the limitations regarding the recited inputs, the desired output, identifiers, identifier matching, and data reordering. Ben-Dor does not provide the missing teachings.

Second, the Examiner has not suggested any benefit that would be gained by the method of Cuticchia/Schena in applying the "alternate means" of Ben-Dor. The number of possible alternate means of analyzing gene mappings is very large, and there is no obvious reason why the means of Ben-Dor would confer a particular advantage to Cuticchia/Schena absent the present application as a guide. In the current office action, the Examiner states "*as line maps are an*

alternate means for mapping the same information using a substitute (are equivalents), it is adequate for an obviousness prior art rejection". Applicant submits that to sustain an obviousness rejection in view of a combination of prior art references the Examiner must show that there is some **motivation** in the art that would cause someone of ordinary skill to combine the references, and that in making the combination, there was a reasonable expectation of success. A proper analysis in this situation requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success... Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442(CAFC 1991). Applicant maintains that there is no suggestion in this case founded in prior art. Accordingly, claims 39 and 85 are not obvious in view of the cited prior art.

The Examiner rejected claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. as applied to claims 1-3, 12-19, 20-37, 40-43, 55-56, 80-83, and 86-89 above, and further in view of Pollack et al. [Nature Genetics, volume 23, 1999, pages 41-46]. Applicant submits that as currently amended, claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 are not obvious in view of the cited prior art.

The Examiner states that Cuticchia teaches all the limitations of claims 44-47, 49, 52-54, 90, 92-93, 95, and 98-101 except those relating to abnormal copy numbers, or the one-to-one correspondences between the third and fourth matrices and the first and second matrices, respectively. The Examiner looks to Schena as teaching the correspondences between matrices, but not that these additional matrices are related to chromosomal copy numbers. The Examiner looks to Pollack for the missing teachings. The Examiner maintains that it would have been obvious to "*to modify the chromosomal mapping techniques of Cuticchia et al. and Schena et al., by use of the color coded heat map plots of Pollack et al. wherein the motivation would have been that the use of such plots allow more conveniently acquired and well resolved data [see*

lines 13-17 of abstract on page 41 and Figure 5a of Pollack et al.]" and to further *"modify differential gene expression to analyze abnormalities as in Cuticchia et al. and Schena et al. by use of the disease analysis by chromosomal copy number analysis as in Pollack et al. because it is obvious to substitute known elements in the prior art to yield a predictable result*".

As noted above with respect to claims 34 and 80, from which claims 44-47, 49, 52-54, 90 and 92-93 respectively depend, the combination of Cuticchia and Schena fails to teach the limitations regarding the recited inputs, the desired output, identifiers, identifier matching, data reordering, or the details regarding the row and column data, normal and abnormal tissue, and the matching and displaying being performed with regard to two matrices that are divided out from a single original matrix. Pollack does not provide the missing teachings. Accordingly, Applicant submits that claims 44-47, 49, 52-54, 90 and 92-93 44, 46-47, 90 and 92-93 are not obvious in view of the cited prior art.

Claim 45 additionally requires that the chromosomal copy number abnormality data be displayed in third and fourth matrices, wherein each value in the third matrix is matched with the expression value in the first matrix having the same row and column location, and wherein each value in the fourth matrix is matched with the expression value in the second matrix having the same row and column location. The Examiner points to Figures 1 and 2 of Schena for this teaching, identifying the "matrices" in Figure 1 as first and second matrices and those in Figure 2 as the third and fourth matrices. However, the data in the "third" matrix relates to data from both "+ Heat Shock" and "-Heat Shock" experiments, i.e. to both first and second matrices, and the data in the "fourth" matrix relates to data from another pair of experiments involving Phorbol Ester, that are not shown anywhere in matrix form, and are certainly not shown in the second matrix. Accordingly, there are additional grounds for allowing claim 45.

Claims 46 and 92 also require that the chromosomal copy number abnormality data be provided in columns interlaced with the columns of expression data in the first and second matrices. The Examiner points to Cuticchia (paragraph bridging columns 1-2 on page 471) as providing this teaching. The cited passage teaches that data may be added to a database, to enter

comments or other general information about clones, but it does not teach that data is provided in interlaced columns in matrices as required by the claim. Accordingly, there are additional grounds for allowing claims 46 and 92.

Claims 53 and 54 depend from claim 45 through claim 49 and include additional limitations corresponding to those of claim 42 and 43 respectively, regarding relevance density scores and filtering. As noted above with respect to claims 42 and 43, the combination of Cuticchia/Schena does not teach the additional limitations Pollack does not provide the missing teachings. Accordingly, there are additional grounds for allowing claims 53 and 54.

Claim 101 has been rewritten to recite several limitations corresponding to those of currently amended claims 1 and 80. As noted above with respect to claims 1 and 80, the combination of Cuticchia and Schena fails to teach the limitations regarding the displayed output or the matching of received identifiers with predefined identifiers. Pollack does not provide the missing teachings. Claim 101 additionally includes limitations corresponding to those of claim 45. As noted above with respect to claim 45, the cited prior art does not teach these additional limitations. Accordingly, Applicant submits that claim 101 and the claims dependent therefrom are not obvious in view of the cited prior art.

Claims 95 and 98-100 depend from claim 101 and include additional limitations corresponding to those of claims 36, 39, 42 and 43. As noted above with respect to claims 36, 39, 42, and 43, the combination of Cuticchia and Schena does not provide the additional teachings regarding relevance scores, p-values, density scores and filtering. Pollack does not provide the missing teachings. Accordingly, there are additional grounds for allowing claims 95 and 98-100.

The Examiner rejected claims 50 and 96 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of McCully [US Patent 4,383,994 issued 17 May 1983; filed 19 January 1982]. Applicant submits that as currently amended, claims 50 and 96 are not obvious in

view of the cited prior art.

The Examiner states that the combination of Cuticchia Schena and Pollack teaches all the limitations of claims 50 and 96 except for requiring that the relevance score comprise a "p value" and the relevance score be displayed as a valued calculated by (-log p value). The Examiner looks to McCully for the additional limitations. The Examiner maintains that it would have been obvious to apply the teachings of McCully to those of Cuticchia/Schena to provide "improved and more advanced statistical analysis".

First, as noted above with respect to claims 1 and 101, from which claims 50 and 96 respectively depend, the combination of Cuticchia and Schena fails to teach several of the base claim limitations. In the case of claim 50, which also depends from claim 49,the combination of Cuticchia and Schena also fails to teach the limitations of that intervening claim 49. Neither Pollack nor McCully provide the missing teachings.

Second, the additional limitations of claims 50 and 96 correspond to those of claim 38. As discussed above with respect to claim 38, the combination of Cuticchia and Schena fails to teach the requirement that a relevance score be calculated for at least one row of the matrices by comparing expression values in the first matrix with expression values in the second matrix, and displaying at least one calculated relevance score along side the row to which each pertains. Neither Pollack nor McCully provide the missing teachings. Accordingly, there are additional grounds for allowing claims 50 and 96.

The Examiner rejected claims 48, 51, 94, and 97 under 35 U.S.C. 103(a) as being unpatentable over Cuticchia et al. in view of Schena et al. in view of Pollack et al. as applied to claims 1-3, 12-37, 40-47, 49, 52-56, 80-83, 86-89, 92-93, 95, and 98-101 above, and further in view of Ben-Dor et al. [Genome Research, 2000, volume 10, pages 365-378]. Applicant submits that as currently amended, claims 48, 51, 94, and 97 are not obvious in view of the cited prior art.

The Examiner states that the combination of Cuticchia, Schena and Pollack teaches all the limitations of claims 48, 51, 94, and 97 except for the use of line maps. The Examiner maintains that it would have been obvious to apply the teachings of Ben-Dor to the method of Partridge/Reeves as "an alternate means of analyzing the mappings of chromosomes".

As noted above with respect to claims 44 and 90, from which claims 48 and 94 respectively depend, the combination of Cuticchia and Schena fails to teach the base claim limitations regarding the recited inputs, the desired output, identifiers, identifier matching, data reordering, or the details regarding the row and column data, normal and abnormal tissue, and the matching and displaying being performed with regard to two matrices that are divided out from a single original matrix. Neither Pollack nor Ben-Dor provide the missing teachings. In addition, the Examiner has not pointed to any advantage in using this alternate means of analyzing the mappings over any of the other possible alternate means in the prior art, absence the present application as a guide. Accordingly, Applicant submits that claims 48 and 94 are not obvious in view of the cited prior art.

As noted above with respect to claim 34 from which claim 51 depends through claim 49, the combination of Cuticchia and Schena does not teach the claim limitations regarding the recited inputs, the desired output, identifiers, identifier matching, data reordering, or the details regarding the row and column data, normal and abnormal tissue, and the matching and displaying being performed with regard to two matrices that are divided out from a single original matrix. Neither Pollack nor Ben-Dor provide the missing teachings. Accordingly, Applicant submits that claim 51 is not obvious in view of the cited prior art.

As noted above with respect to claim 95, from which claim 97 depends, the limitations corresponding to those of claim 36 regarding relevance scores are not taught by the combination of Cuticchia, Schena and Pollack. Ben-Dor does not provide the missing teachings. Accordingly, Applicant submits that claim 97 is not obvious in view of the cited prior art.

Respectfully Submitted,

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